

SEQUENCE LISTING

<110> Hopf, Carsten
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Ruffner, Heinz

<120> Treatment of Neurodegenerative Diseases by the Use of GPR49

<130> 50125/113001

<140> US 10/587,159

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<150> PCT/EP2004/013539

<151> 2004-11-29

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<151> 2004-01-29

<160> 4

<170> PatentIn version 3.3

<210> 1

<211> 21

<212> DNA

<213> Artificial sequence

<220>

<223> designed siRNA

<400> 1

aacagcagta tggacgacct t

21

<210> 2

<211> 907

<212> PRT

<213> Homo sapiens

<400> 2

Met Asp Thr Ser Arg Leu Gly Val Leu Leu Ser Leu Pro Val Leu Leu

1

5

10

15

Gln Leu Ala Thr Gly Gly Ser Ser Pro Arg Ser Gly Val Leu Leu Arg
 20 25 30

Gly Cys Pro Thr His Cys His Cys Glu Pro Asp Gly Arg Met Leu Leu
 35 40 45

Arg Val Asp Cys Ser Asp Leu Gly Leu Ser Glu Leu Pro Ser Asn Leu
 50 55 60

Ser Val Phe Thr Ser Tyr Leu Asp Leu Ser Met Asn Asn Ile Ser Gln
 65 70 75 80

Leu Leu Pro Asn Pro Leu Pro Ser Leu Arg Phe Leu Glu Glu Leu Arg
 85 90 95

Leu Ala Gly Asn Ala Leu Thr Tyr Ile Pro Lys Gly Ala Phe Thr Gly
 100 105 110

Leu Tyr Ser Leu Lys Val Leu Met Leu Gln Asn Asn Gln Leu Arg His
 115 120 125

Val Pro Thr Glu Ala Leu Gln Asn Leu Arg Ser Leu Gln Ser Leu Arg
 130 135 140

Leu Asp Ala Asn His Ile Ser Tyr Val Pro Pro Ser Cys Phe Ser Gly
 145 150 155 160

Leu His Ser Leu Arg His Leu Trp Leu Asp Asp Asn Ala Leu Thr Glu
 165 170 175

Ile Pro Val Gln Ala Phe Arg Ser Leu Ser Ala Leu Gln Ala Met Thr
 180 185 190

Leu Ala Leu Asn Lys Ile His His Ile Pro Asp Tyr Ala Phe Gly Asn
 195 200 205

Leu Ser Ser Leu Val Val Leu His Leu His Asn Asn Arg Ile His Ser
 210 215 220

Leu Gly Lys Lys Cys Phe Asp Gly Leu His Ser Leu Glu Thr Leu Asp
 225 230 235 240

Leu Asn Tyr Asn Asn Leu Asp Glu Phe Pro Thr Ala Ile Arg Thr Leu
245 250 255

Ser Asn Leu Lys Glu Leu Gly Phe His Ser Asn Asn Ile Arg Ser Ile
260 265 270

Pro Glu Lys Ala Phe Val Gly Asn Pro Ser Leu Ile Thr Ile His Phe
275 280 285

Tyr Asp Asn Pro Ile Gln Phe Val Gly Arg Ser Ala Phe Gln His Leu
290 295 300

Pro Glu Leu Arg Thr Leu Thr Leu Asn Gly Ala Ser Gln Ile Thr Glu
305 310 315 320

Phe Pro Asp Leu Thr Gly Thr Ala Asn Leu Glu Ser Leu Thr Leu Thr
325 330 335

Gly Ala Gln Ile Ser Ser Leu Pro Gln Thr Val Cys Asn Gln Leu Pro
340 345 350

Asn Leu Gln Val Leu Asp Leu Ser Tyr Asn Leu Leu Glu Asp Leu Pro
355 360 365

Ser Phe Ser Val Cys Gln Lys Leu Gln Lys Ile Asp Leu Arg His Asn
370 375 380

Glu Ile Tyr Glu Ile Lys Val Asp Thr Phe Gln Gln Leu Leu Ser Leu
385 390 395 400

Arg Ser Leu Asn Leu Ala Trp Asn Lys Ile Ala Ile Ile His Pro Asn
405 410 415

Ala Phe Ser Thr Leu Pro Ser Leu Ile Lys Leu Asp Leu Ser Ser Asn
420 425 430

Leu Leu Ser Ser Phe Pro Ile Thr Gly Leu His Gly Leu Thr His Leu
435 440 445

Lys Leu Thr Gly Asn His Ala Leu Gln Ser Leu Ile Ser Ser Glu Asn
450 455 460

Phe Pro Glu Leu Lys Val Ile Glu Met Pro Tyr Ala Tyr Gln Cys Cys

465					470					475				480	
Ala	Phe	Gly	Val	Cys	Glu	Asn	Ala	Tyr	Lys	Ile	Ser	Asn	Gln	Trp	Asn
				485					490					495	
Lys	Gly	Asp	Asn	Ser	Ser	Met	Asp	Asp	Leu	His	Lys	Lys	Asp	Ala	Gly
			500					505					510		
Met	Phe	Gln	Ala	Gln	Asp	Glu	Arg	Asp	Leu	Glu	Asp	Phe	Leu	Leu	Asp
		515					520					525			
Phe	Glu	Glu	Asp	Leu	Lys	Ala	Leu	His	Ser	Val	Gln	Cys	Ser	Pro	Ser
	530					535					540				
Pro	Gly	Pro	Phe	Lys	Pro	Cys	Glu	His	Leu	Leu	Asp	Gly	Trp	Leu	Ile
545					550					555					560
Arg	Ile	Gly	Val	Trp	Thr	Ile	Ala	Val	Leu	Ala	Leu	Thr	Cys	Asn	Ala
				565					570					575	
Leu	Val	Thr	Ser	Thr	Val	Phe	Arg	Ser	Pro	Leu	Tyr	Ile	Ser	Pro	Ile
			580					585					590		
Lys	Leu	Leu	Ile	Gly	Val	Ile	Ala	Ala	Val	Asn	Met	Leu	Thr	Gly	Val
		595					600					605			
Ser	Ser	Ala	Val	Leu	Ala	Gly	Val	Asp	Ala	Phe	Thr	Phe	Gly	Ser	Phe
	610					615					620				
Ala	Arg	His	Gly	Ala	Trp	Trp	Glu	Asn	Gly	Val	Gly	Cys	His	Val	Ile
625					630					635					640
Gly	Phe	Leu	Ser	Ile	Phe	Ala	Ser	Glu	Ser	Ser	Val	Phe	Leu	Leu	Thr
				645					650					655	
Leu	Ala	Ala	Leu	Glu	Arg	Gly	Phe	Ser	Val	Lys	Tyr	Ser	Ala	Lys	Phe
			660					665					670		
Glu	Thr	Lys	Ala	Pro	Phe	Ser	Ser	Leu	Lys	Val	Ile	Ile	Leu	Leu	Cys
		675					680					685			
Ala	Leu	Leu	Ala	Leu	Thr	Met	Ala	Ala	Val	Pro	Leu	Leu	Gly	Gly	Ser
						695					700				

Lys Tyr Gly Ala Ser Pro Leu Cys Leu Pro Leu Pro Phe Gly Glu Pro
705 710 715 720

Ser Thr Met Gly Tyr Met Val Ala Leu Ile Leu Leu Asn Ser Leu Cys
725 730 735

Phe Leu Met Met Thr Ile Ala Tyr Thr Lys Leu Tyr Cys Asn Leu Asp
740 745 750

Lys Gly Asp Leu Glu Asn Ile Trp Asp Cys Ser Met Val Lys His Ile
755 760 765

Ala Leu Leu Leu Phe Thr Asn Cys Ile Leu Asn Cys Pro Val Ala Phe
770 775 780

Leu Ser Phe Ser Ser Leu Ile Asn Leu Thr Phe Ile Ser Pro Glu Val
785 790 795 800

Ile Lys Phe Ile Leu Leu Val Val Val Pro Leu Pro Ala Cys Leu Asn
805 810 815

Pro Leu Leu Tyr Ile Leu Phe Asn Pro His Phe Lys Glu Asp Leu Val
820 825 830

Ser Leu Arg Lys Gln Thr Tyr Val Trp Thr Arg Ser Lys His Pro Ser
835 840 845

Leu Met Ser Ile Asn Ser Asp Asp Val Glu Lys Gln Ser Cys Asp Ser
850 855 860

Thr Gln Ala Leu Val Thr Phe Thr Ser Ser Ser Ile Thr Tyr Asp Leu
865 870 875 880

Pro Pro Ser Ser Val Pro Ser Pro Ala Tyr Pro Val Thr Glu Ser Cys
885 890 895

His Leu Ser Ser Val Ala Phe Val Pro Cys Leu
900 905

<210> 3
<211> 828
<212> PRT

<213> Homo sapiens

<400> 3

Met Arg Leu Glu Gly Glu Gly Arg Ser Ala Arg Ala Gly Gln Asn Leu
1 5 10 15

Ser Arg Ala Gly Ser Ala Arg Arg Gly Ala Pro Arg Asp Leu Ser Met
20 25 30

Asn Asn Leu Thr Glu Leu Gln Pro Gly Leu Phe His His Leu Arg Phe
35 40 45

Leu Glu Glu Leu Arg Leu Ser Gly Asn His Leu Ser His Ile Pro Gly
50 55 60

Gln Ala Phe Ser Gly Leu Tyr Ser Leu Lys Ile Leu Met Leu Gln Asn
65 70 75 80

Asn Gln Leu Gly Gly Ile Pro Ala Glu Ala Leu Trp Glu Leu Pro Ser
85 90 95

Leu Gln Ser Leu Asp Leu Asn Tyr Asn Lys Leu Gln Glu Phe Pro Val
100 105 110

Ala Ile Arg Thr Leu Gly Arg Leu Gln Glu Leu Gly Phe His Asn Asn
115 120 125

Asn Ile Lys Ala Ile Pro Glu Lys Ala Phe Met Gly Asn Pro Leu Leu
130 135 140

Gln Thr Ile His Phe Tyr Asp Asn Pro Ile Gln Phe Val Gly Arg Ser
145 150 155 160

Ala Phe Gln Tyr Leu Pro Lys Leu His Thr Leu Ser Leu Asn Gly Ala
165 170 175

Met Asp Ile Gln Glu Phe Pro Asp Leu Lys Gly Thr Thr Ser Leu Glu
180 185 190

Ile Leu Thr Leu Thr Arg Ala Gly Ile Arg Leu Leu Pro Ser Gly Met
195 200 205

Cys Gln Gln Leu Pro Arg Leu Arg Val Leu Glu Leu Ser His Asn Gln

210	215	220
Ile Glu Glu Leu Pro Ser Leu His Arg Cys Gln Lys Leu Glu Glu Ile 225 230 235 240		
Gly Leu Gln His Asn Arg Ile Trp Glu Ile Gly Ala Asp Thr Phe Ser 245 250 255		
Gln Leu Ser Ser Leu Gln Ala Leu Asp Leu Ser Trp Asn Ala Ile Arg 260 265 270		
Ser Ile His Pro Glu Ala Phe Ser Thr Leu His Ser Leu Val Lys Leu 275 280 285		
Asp Leu Thr Asp Asn Gln Leu Thr Thr Leu Pro Leu Ala Gly Leu Gly 290 295 300		
Gly Leu Met His Leu Lys Leu Lys Gly Asn Leu Ala Leu Ser Gln Ala 305 310 315 320		
Phe Ser Lys Asp Ser Phe Pro Lys Leu Arg Ile Leu Glu Val Pro Tyr 325 330 335		
Ala Tyr Gln Cys Cys Pro Tyr Gly Met Cys Ala Ser Phe Phe Lys Ala 340 345 350		
Ser Gly Gln Trp Glu Ala Glu Asp Leu His Leu Asp Asp Glu Glu Ser 355 360 365		
Ser Lys Arg Pro Leu Gly Leu Leu Ala Arg Gln Ala Glu Asn His Tyr 370 375 380		
Asp Gln Asp Leu Asp Glu Leu Gln Leu Glu Met Glu Asp Ser Lys Pro 385 390 395 400		
His Pro Ser Val Gln Cys Ser Pro Thr Pro Gly Pro Phe Lys Pro Cys 405 410 415		
Glu Tyr Leu Phe Glu Ser Trp Gly Ile Arg Leu Ala Val Trp Ala Ile 420 425 430		
Val Leu Leu Ser Val Leu Cys Asn Gly Leu Val Leu Leu Thr Val Phe 435 440 445		

Ala Gly Gly Pro Val Pro Leu Pro Pro Val Lys Phe Val Val Gly Ala
450 455 460

Ile Ala Gly Ala Asn Thr Leu Thr Gly Ile Ser Cys Gly Leu Leu Ala
465 470 475 480

Ser Val Asp Ala Leu Thr Phe Gly Gln Phe Ser Glu Tyr Gly Ala Arg
485 490 495

Trp Glu Thr Gly Leu Gly Cys Arg Ala Thr Gly Phe Leu Ala Val Leu
500 505 510

Gly Ser Glu Ala Ser Val Leu Leu Leu Thr Leu Ala Ala Val Gln Cys
515 520 525

Ser Val Ser Val Ser Cys Val Arg Ala Tyr Gly Lys Ser Pro Ser Leu
530 535 540

Gly Ser Val Arg Ala Gly Val Leu Gly Cys Leu Ala Leu Ala Gly Leu
545 550 555 560

Ala Ala Ala Leu Pro Leu Ala Ser Val Gly Glu Tyr Gly Ala Ser Pro
565 570 575

Leu Cys Leu Pro Tyr Ala Pro Pro Glu Gly Gln Pro Ala Ala Leu Gly
580 585 590

Phe Thr Val Ala Leu Val Met Met Asn Ser Phe Cys Phe Leu Val Val
595 600 605

Ala Gly Ala Tyr Ile Lys Leu Tyr Cys Asp Leu Pro Arg Gly Asp Phe
610 615 620

Glu Ala Val Trp Asp Cys Ala Met Val Arg His Val Ala Trp Leu Ile
625 630 635 640

Phe Ala Asp Gly Leu Leu Tyr Cys Pro Val Ala Phe Leu Ser Phe Ala
645 650 655

Ser Met Leu Gly Leu Phe Pro Val Thr Pro Glu Ala Val Lys Ser Val
660 665 670

Leu Leu Val Val Leu Pro Leu Pro Ala Cys Leu Asn Pro Leu Leu Tyr
675 680 685

Leu Leu Phe Asn Pro His Phe Arg Asp Asp Leu Arg Arg Leu Arg Pro
690 695 700

Arg Ala Gly Asp Ser Gly Pro Leu Ala Tyr Ala Ala Ala Gly Glu Leu
705 710 715 720

Glu Lys Ser Ser Cys Asp Ser Thr Gln Ala Leu Val Ala Phe Ser Asp
725 730 735

Val Asp Leu Ile Leu Glu Ala Ser Glu Ala Gly Arg Pro Pro Gly Leu
740 745 750

Glu Thr Tyr Gly Phe Pro Ser Val Thr Leu Ile Ser Cys Gln Gln Pro
755 760 765

Gly Ala Pro Arg Leu Glu Gly Ser His Cys Val Glu Pro Glu Gly Asn
770 775 780

His Phe Gly Asn Pro Gln Pro Ser Met Asp Gly Glu Leu Leu Leu Arg
785 790 795 800

Ala Glu Gly Ser Thr Pro Ala Gly Gly Gly Leu Ser Gly Gly Gly Gly
805 810 815

Phe Gln Pro Ser Gly Leu Ala Phe Ala Ser His Val
820 825

<210> 4
<211> 955
<212> PRT
<213> Homo sapiens

<400> 4

Met Pro Gly Pro Leu Gly Leu Leu Cys Phe Leu Ala Leu Gly Leu Leu
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Gly Ser Ala Gly Pro Ser Gly Ala Ala Pro Pro Leu Cys Ala Ala Pro
20 25 30

Cys Ser Cys Asp Gly Asp Arg Arg Val Asp Cys Ser Gly Lys Gly Leu

35	40	45															
Thr	Ala	Val	Pro	Glu	Gly	Leu	Ser	Ala	Phe	Thr	Gln	Ala	Leu	Asp	Ile		
50						55					60						
Ser	Met	Asn	Asn	Ile	Thr	Gln	Leu	Pro	Glu	Asp	Ala	Phe	Lys	Asn	Phe		
65					70					75					80		
Pro	Phe	Leu	Glu	Glu	Leu	Gln	Leu	Ala	Gly	Asn	Asp	Leu	Ser	Phe	Ile		
				85					90					95			
His	Pro	Lys	Ala	Leu	Ser	Gly	Leu	Lys	Glu	Leu	Lys	Val	Leu	Thr	Leu		
			100					105						110			
Gln	Asn	Asn	Gln	Leu	Lys	Thr	Val	Pro	Ser	Glu	Ala	Ile	Arg	Gly	Leu		
		115					120						125				
Ser	Ala	Leu	Gln	Ser	Leu	Arg	Leu	Asp	Ala	Asn	His	Ile	Thr	Ser	Val		
	130					135					140						
Pro	Glu	Asp	Ser	Phe	Glu	Gly	Leu	Val	Gln	Leu	Arg	His	Leu	Trp	Leu		
145					150					155					160		
Asp	Asp	Asn	Ser	Leu	Thr	Glu	Val	Pro	Val	His	Pro	Leu	Ser	Asn	Leu		
				165					170					175			
Pro	Thr	Leu	Gln	Ala	Leu	Thr	Leu	Ala	Leu	Asn	Lys	Ile	Ser	Ser	Ile		
			180					185					190				
Pro	Asp	Phe	Ala	Phe	Thr	Asn	Leu	Ser	Ser	Leu	Val	Val	Leu	His	Leu		
		195					200					205					
His	Asn	Asn	Lys	Ile	Arg	Ser	Leu	Ser	Gln	His	Cys	Phe	Asp	Gly	Leu		
	210					215					220						
Asp	Asn	Leu	Glu	Thr	Leu	Asp	Leu	Asn	Tyr	Asn	Asn	Leu	Gly	Glu	Phe		
225					230					235					240		
Pro	Gln	Ala	Ile	Lys	Ala	Leu	Pro	Ser	Leu	Lys	Glu	Leu	Gly	Phe	His		
				245					250					255			
Ser	Asn	Ser	Ile	Ser	Val	Ile	Pro	Asp	Gly	Ala	Phe	Asp	Gly	Asn	Pro		
			260					265					270				

Leu Leu Arg Thr Ile His Leu Tyr Asp Asn Pro Leu Ser Phe Val Gly
275 280 285

Asn Ser Ala Phe His Asn Leu Ser Asp Leu His Ser Leu Val Ile Arg
290 295 300

Gly Ala Ser Met Val Gln Gln Phe Pro Asn Leu Thr Gly Thr Val His
305 310 315 320

Leu Glu Ser Leu Thr Leu Thr Gly Thr Lys Ile Ser Ser Ile Pro Asn
325 330 335

Asn Leu Cys Gln Glu Gln Lys Met Leu Arg Thr Leu Asp Leu Ser Tyr
340 345 350

Asn Asn Ile Arg Asp Leu Pro Ser Phe Asn Gly Cys His Ala Leu Glu
355 360 365

Glu Ile Ser Leu Gln Arg Asn Gln Ile Tyr Gln Ile Lys Glu Gly Thr
370 375 380

Phe Gln Gly Leu Ile Ser Leu Arg Ile Leu Asp Leu Ser Arg Asn Leu
385 390 395 400

Ile His Glu Ile His Ser Arg Ala Phe Ala Thr Leu Gly Pro Ile Thr
405 410 415

Asn Leu Asp Val Ser Phe Asn Glu Leu Thr Ser Phe Pro Thr Glu Gly
420 425 430

Leu Asn Gly Leu Asn Gln Leu Lys Leu Val Gly Asn Phe Lys Leu Lys
435 440 445

Glu Ala Leu Ala Ala Lys Asp Phe Val Asn Leu Arg Ser Leu Ser Val
450 455 460

Pro Tyr Ala Tyr Gln Cys Cys Ala Phe Trp Gly Cys Asp Ser Tyr Ala
465 470 475 480

Asn Leu Asn Thr Glu Asp Asn Ser Leu Gln Asp His Ser Val Ala Gln
485 490 495

Glu Lys Gly Lys Cys Met Ser Thr Ala Asp Ala Ala Asn Val Thr Ser
500 505 510

Thr Leu Glu Asn Glu Glu His Ser Gln Ile Ile Ile His Cys Thr Pro
515 520 525

Ser Thr Gly Ala Phe Lys Pro Cys Glu Tyr Leu Leu Gly Ser Trp Met
530 535 540

Ile Arg Leu Thr Val Trp Phe Ile Phe Leu Val Ala Leu Phe Phe Asn
545 550 555 560

Leu Leu Val Ile Leu Thr Thr Phe Ala Ser Cys Thr Ser Leu Pro Ser
565 570 575

Ser Lys Leu Phe Ile Gly Leu Ile Ser Val Ser Asn Leu Phe Met Gly
580 585 590

Ile Tyr Thr Gly Ile Leu Thr Phe Leu Asp Ala Val Ser Trp Gly Arg
595 600 605

Phe Ala Glu Phe Gly Ile Trp Trp Glu Thr Gly Ser Gly Cys Lys Val
610 615 620

Ala Gly Phe Leu Ala Val Phe Ser Ser Glu Ser Ala Ile Phe Leu Leu
625 630 635 640

Met Leu Ala Thr Val Glu Arg Ser Leu Ser Ala Lys Asp Ile Met Lys
645 650 655

Asn Gly Lys Ser Asn His Leu Lys Gln Phe Arg Val Ala Ala Leu Leu
660 665 670

Ala Phe Leu Gly Ala Thr Val Ala Gly Cys Phe Pro Leu Phe His Arg
675 680 685

Gly Glu Tyr Ser Ala Ser Pro Leu Cys Leu Pro Phe Pro Thr Gly Glu
690 695 700

Thr Pro Ser Leu Gly Phe Thr Val Thr Leu Val Leu Leu Asn Ser Leu
705 710 715 720

Ala Phe Leu Leu Met Ala Val Ile Tyr Thr Lys Leu Tyr Cys Asn Leu
725 730 735

Glu Lys Glu Asp Leu Ser Glu Asn Ser Gln Ser Ser Met Ile Lys His
740 745 750

Val Ala Trp Leu Ile Phe Thr Asn Cys Ile Phe Phe Cys Pro Val Ala
755 760 765

Phe Phe Ser Phe Ala Pro Leu Ile Thr Ala Ile Ser Ile Ser Pro Glu
770 775 780

Ile Met Lys Ser Val Thr Leu Ile Phe Phe Pro Leu Pro Ala Cys Leu
785 790 795 800

Asn Pro Val Leu Tyr Val Phe Phe Asn Pro Lys Phe Lys Glu Asp Trp
805 810 815

Lys Leu Leu Lys Arg Arg Val Thr Lys Lys Ser Gly Ser Val Ser Val
820 825 830

Ser Ile Ser Ser Gln Gly Gly Cys Leu Glu Gln Asp Phe Tyr Tyr Asp
835 840 845

Cys Gly Met Tyr Ser His Leu Gln Gly Asn Leu Thr Val Cys Asp Cys
850 855 860

Cys Glu Ser Phe Leu Leu Thr Lys Pro Val Ser Cys Lys His Leu Ile
865 870 875 880

Lys Ser His Ser Cys Pro Ala Leu Ala Val Ala Ser Cys Gln Arg Pro
885 890 895

Glu Gly Tyr Trp Ser Asp Cys Gly Thr Gln Ser Ala His Ser Asp Tyr
900 905 910

Ala Asp Glu Glu Asp Ser Phe Val Ser Asp Ser Ser Asp Gln Val Gln
915 920 925

Ala Cys Gly Arg Ala Cys Phe Tyr Gln Ser Arg Gly Phe Pro Leu Val
930 935 940

Arg Tyr Ala Tyr Asn Leu Pro Arg Val Lys Asp

945

950

955